

=> d his 1

(FILE 'HCAPLUS' ENTERED AT 08:17:06 ON 22 JUN 2004)

L25 13 S L3-L14 OR L16-L18 OR L20 OR L21 OR L23 OR L24

=> d que 125

L1 5 SEA FILE=REGISTRY LEHDGIN/SQSP
 L2 5 SEA FILE=REGISTRY L1 AND SQL<=150
 L3 5 SEA FILE=HCAPLUS L2
 L4 5 SEA FILE=HCAPLUS FLUOR? AND L3
 L5 3 SEA FILE=HCAPLUS CASPASE? AND L3
 L6 0 SEA FILE=HCAPLUS FRET AND L3
 L7 1 SEA FILE=HCAPLUS FLUORESC?(3A)RESONAN? AND L3
 L8 1 SEA FILE=HCAPLUS QUENCH? AND L3
 L9 1 SEA FILE=HCAPLUS L7 AND L8
 L10 5 SEA FILE=HCAPLUS ?RHODAMIN? AND L3
 L11 2 SEA FILE=HCAPLUS ?XANTHYLIUM? AND L3
 L12 4 SEA FILE=HCAPLUS ?COUMARIN? AND L3
 L13 0 SEA FILE=HCAPLUS ?CARBOCYANIN? AND L3
 L14 4 SEA FILE=HCAPLUS ?CYANIN? AND L3
 L15 98 SEA FILE=HCAPLUS CASPASE? AND ?RHODAMIN?
 L16 5 SEA FILE=HCAPLUS L15 AND QUENCH?
 L17 2 SEA FILE=HCAPLUS L15 AND FLUOR?(3A)RESONAN?
 L18 1 SEA FILE=HCAPLUS CASPASE? AND ?XANTHYLIUM?
 L19 93 SEA FILE=HCAPLUS CASPASE? AND ?COUMARIN?
 L20 0 SEA FILE=HCAPLUS L19 AND QUENCH?
 L21 2 SEA FILE=HCAPLUS L19 AND FLUOR? (3A)RESONAN?
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 L23 0 SEA FILE=HCAPLUS L22 AND QUENCH?
 L24 1 SEA FILE=HCAPLUS L22 AND FLUOR? (3A)RESONAN?
 L25 13 SEA FILE=HCAPLUS (L3 OR L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR
 L10 OR L11 OR L12 OR L13 OR L14) OR (L16 OR L17 OR L18) OR L20
 OR L21 OR L23 OR L24

=> d iall 125 1-13

L25 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:414513 HCAPLUS

DOCUMENT NUMBER: 140:419882

ENTRY DATE: Entered STN: 21 May 2004

TITLE: **Fluorescent** peptide substrates for the
detection of enzyme activity in biological samples

INVENTOR(S): Packard, Beverly S.; Komoriya, Akira

PATENT ASSIGNEE(S): OncoImmunin, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 114 pp., Cont.-in-part of Appl.
No. PCT/US00/24882.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: C12Q001-37

SECONDARY: G01N033-573; C07K014-00

US PATENT CLASSIF.: 435023000; 530324000

CLASSIFICATION: 7-1 (Enzymes)

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2004096926      A1  20040520      US 2001-874350      20010604
US 6037137          A   20000314      US 1997-802981      19970220
WO 9837226          A1  19980827      WO 1998-US3000      19980220
W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
    DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
    KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
    NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
    UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW:  GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
    FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
    GA, GN, ML, MR, NE, SN, TD, TG
WO 2001018238      A1  20010315      WO 2000-US24882      20000911
W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
    CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
    HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
    LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
    SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
    YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW:  GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
    DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
    CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:      US 1997-802981      A2 19970220
                                WO 1998-US3000      A2 19980220
                                US 1999-394019      A2 19990910
                                WO 2000-US24882      A2 20000911

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ABSTRACT:

The present invention provides for novel reagents whose **fluorescence** increases in the presence of particular proteases. The reagents comprise a characteristically folded peptide backbone conjugated to two *****fluorophores***** such that the **fluorophores** are located opposite sides of a cleavage site. When the folded peptide is cleaved, as by digestion with a protease, the **fluorophores** provide a high intensity *****fluorescent***** signal at a visible wavelength. Because of their high specificity and their high **fluorescence** signal in the visible wavelengths, these protease indicators are particularly well suited for detection of protease activity in biol. samples, in particular in frozen tissue sections. In one example, the protease indicator having the formula F1-Asp-Ala-Ile-Pro-Nle-Ser-Ile-Pro-Cys-F2, where F1 is a donor *****fluorophore***** (5-carboxytetramethylrhodamine) linked to aspartic acid via the α -amino group and F2 is an acceptor *****fluorophore***** (rhodamine X acetamide (R492)) linked via the sulfhydryl group of the cysteine, exhibits changes in emission spectrum after addn of an elastase protease. Thus this invention also provides for methods of detecting protease activity in situ in frozen sections.

SUPPL. TERM: **fluorescent** peptide substrate enzyme detection;
 protease detection **fluorescent** peptide substrate;
 elastase detection **fluorescent** peptide substrate

INDEX TERM: Peptides, uses
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (doubly-labeled; **fluorescent** peptide substrates
 for the detection of enzyme activity in biol. samples)

INDEX TERM: Cytometry
 (flow; **fluorescent** peptide substrates for the
 detection of enzyme activity in biol. samples)

INDEX TERM: Absorption spectroscopy
 Animal tissue

Blood analysis
 Cyanine dyes
 Fluorescence microscopy
 Fluorescent indicators
 Fluorometry
 High throughput screening
 Lymph
 Saliva
 Urine analysis
 (**fluorescent** peptide substrates for the
 detection of enzyme activity in biol. samples)
 INDEX TERM: Enzymes, analysis
 ROLE: ANT (Analyte); ANST (Analytical study)
 (**fluorescent** peptide substrates for the
 detection of enzyme activity in biol. samples)
 INDEX TERM: Functional groups
 (hydrophobic; **fluorescent** peptide substrates
 for the detection of enzyme activity in biol. samples)
 INDEX TERM: 247187-60-6
 ROLE: BSU (Biological study, unclassified); BIOL (Biological
 study)
 (apoptosis blocker; **fluorescent** peptide
 substrates for the detection of enzyme activity in biol.
 samples)
 INDEX TERM: 171978-35-1
 ROLE: BSU (Biological study, unclassified); BIOL (Biological
 study)
 (apoptosis-related protease inhibitor;
 fluorescent peptide substrates for the detection
 of enzyme activity in biol. samples)
 INDEX TERM: 212268-97-8 212268-98-9 212268-99-0 212269-00-6
 212269-01-7 212269-02-8 212269-03-9 212269-04-0
 212269-05-1 212269-06-2 212269-07-3 212269-08-4
 212269-09-5 212269-10-8
 ROLE: ARG (Analytical reagent use); BSU (Biological study,
 unclassified); ANST (Analytical study); BIOL (Biological
 study); USES (Uses)
 (cellular uptake; **fluorescent** peptide
 substrates for the detection of enzyme activity in biol.
 samples)
 INDEX TERM: 9001-92-7, Proteinase 9004-06-2, Elastase 169592-56-7,
 Caspase 3 179241-78-2, **Caspase 8**
 182372-15-2, **Caspase 6** 186322-81-6,
 Caspase 189258-14-8, **Caspase 7**
 ROLE: ANT (Analyte); ANST (Analytical study)
 (**fluorescent** peptide substrates for the
 detection of enzyme activity in biol. samples)
 INDEX TERM: 596-24-7 989-38-8, Rh6G 2768-89-0, **Rhodamine X**
 20571-42-0 25152-49-2, 9-(2-Carboxyphenyl)-2,7-dimethyl-
 3,6-bis(ethylamino)**xanthylum** 91809-66-4D,
 halides 91809-67-5D, halides 125481-77-8 135926-08-8
 198978-94-8 199608-29-2D, labeled with 6-TMR and/or DER
 203116-52-3 212207-37-9 212207-40-4 220906-39-8
 222164-84-3, Rh 110 690962-76-6D, halides 690962-77-7
 691868-32-3 691868-33-4 691868-34-5 691868-35-6
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (**fluorescent** peptide substrates for the
 detection of enzyme activity in biol. samples)

INDEX TERM: 413568-29-3, PhiPhiLux 691873-33-3, CaspaLux-3PE
 691873-34-4, CaspaLux-6 **691873-35-5**, CaspaLux-9
 691873-36-6, DCaspaLux-1
 ROLE: ARG (Analytical reagent use); BSU (Biological study,
 unclassified); ANST (Analytical study); BIOL (Biological
 study); USES (Uses)

(**fluorescent** peptide substrates for the
 detection of enzyme activity in biol. samples)

INDEX TERM: 691510-59-5 691510-60-8 691510-61-9 691510-62-0
 691510-63-1 691510-64-2 691510-65-3 691510-66-4
 691510-67-5 691510-68-6 691510-69-7 691510-70-0
 691510-71-1 691510-72-2 691510-73-3 691510-74-4
 691510-75-5 691510-76-6 691510-77-7 691510-78-8
 691510-79-9 691510-80-2 691510-81-3 691510-82-4
 691510-83-5 691510-84-6 691510-85-7 691510-86-8
 691510-87-9 691510-88-0 691510-89-1 691510-90-4
 691510-91-5 691510-92-6 691510-93-7 691510-94-8
 691510-95-9 691510-96-0 691510-97-1 691510-98-2
 691510-99-3 691511-00-9 691511-01-0 691511-02-1
 691511-03-2 691511-04-3 691511-05-4 691511-06-5
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 691511-76-9 691511-77-0 691511-78-1 691511-79-2
 691511-80-5 691511-81-6 691511-82-7 691511-83-8
 691511-84-9 **691511-85-0** 691511-86-1
 691511-87-2 691511-88-3 691511-89-4 691511-90-7
 691511-91-8 691511-92-9 691511-93-0 691511-94-1
 691511-95-2 691511-96-3 691511-97-4 691511-98-5
 691511-99-6 691512-00-2 691512-01-3 691512-02-4
 691512-03-5 691512-04-6

ROLE: PRP (Properties)
 (unclaimed protein sequence; **fluorescent**
 peptide substrates for the detection of enzyme activity
 in biol. samples)

INDEX TERM: 637-84-3 150234-52-9 330153-49-6 330153-50-9
 330574-44-2 330574-45-3 330624-27-6 330624-29-8
 330624-30-1 330624-31-2 330624-32-3 622400-97-9
 691388-69-9 691388-71-3 691388-72-4 691388-73-5
 691388-74-6 691511-48-5

ROLE: PRP (Properties)
 (unclaimed sequence; **fluorescent** peptide
 substrates for the detection of enzyme activity in biol.
 samples)

L25 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:88323 HCAPLUS

DOCUMENT NUMBER: 140:299199

ENTRY DATE: Entered STN: 04 Feb 2004

TITLE: Fluorescence **Quenching**-Based Assays for Hydrolyzing Enzymes. Application of Time-Resolved Fluorometry in Assays for **Caspase**, Helicase, and PhosphataseAUTHOR(S): Karvinen, Jarkko; Laitala, Ville; Maekinen, Maija-Liisa; Mulari, Outi; Tamminen, Johanna; Hermonen, Jorma; Hurskainen, Pertti; Hemmilae, Ilkka
CORPORATE SOURCE: PerkinElmer Life and Analytical Sciences, Wallac Oy, Turku, FIN-20101, FinlandSOURCE: Analytical Chemistry (2004), 76(5), 1429-1436
CODEN: ANCHAM; ISSN: 0003-2700

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 7-1 (Enzymes)

ABSTRACT:

We have developed assay technologies to measure hydrolyzing enzymes based on homogeneous time-resolved fluorescence **quenching** (TruPoint). High sensitivity was obtained using fluorescent europium chelates as labels, internally **quenched** by suitable **quenchers** and released upon enzymic reaction. This approach allows robust and sensitive monitoring of low enzyme activities. The assay technol. and the choice of donor-acceptor pairs were evaluated in three different enzymic assays, a protease related to apoptosis, helicase involved in DNA unwinding, and phosphatase having an important role in cellular signaling cascades. All the assays produced an increasing signal, were sensitive, and had a good dynamic range. There were significant differences in optimized **quenchers** for each of the assays depending on the size, flexibility, and rigidity of the substrates. Also, clear differences in the energy-transfer reactions, their requirements for spectral overlapping, ionic interactions, and energy-transfer distances were found. Each of the enzymic assays was briefly tested in a high-throughput screening environment by analyzing signal dynamics and statistical relevance as Z' factors.

SUPPL. TERM: enzyme assay fluorescence **quenching**
caspase DNA helicase CD45 phosphataseINDEX TERM: Enzymes, analysis
ROLE: ANT (Analyte); ANST (Analytical study)
(DNA helicase; time-resolved fluorometric assays for **caspase**-3, DNA helicase, and CD45 phosphatase employ Eu3+ chelates in conjunction with chromophore **quenchers**)INDEX TERM: Energy transfer
(time-resolved fluorometric assays for **caspase**-3, DNA helicase, and CD45 phosphatase employ Eu3+ chelates in conjunction with chromophore **quenchers**)INDEX TERM: Fluorometry
(time-resolved; time-resolved fluorometric assays for **caspase**-3, DNA helicase, and CD45 phosphatase employ Eu3+ chelates in conjunction with chromophore **quenchers**)INDEX TERM: 169592-56-7, **Caspase**-3 300859-91-0, Protein tyrosine phosphatase CD45
ROLE: ANT (Analyte); ANST (Analytical study)

(time-resolved fluorometric assays for **caspase**
-3, DNA helicase, and CD45 phosphatase employ Eu3+
chelates in conjunction with chromophore
quenchers)

INDEX TERM: 6268-49-1D, Dabcyl, conjugates with peptides and
oligonucleotides 70281-37-7D, **Tetramethylrhodamine**
, conjugates with peptides and oligonucleotides
146368-14-1D, Cy5, conjugates with peptides 247145-23-9D,
AlexaFluor 546, conjugates with peptides 304014-12-8D, QSY
7, conjugates with peptides and oligonucleotides
400051-23-2D, AlexaFluor 647, conjugates with peptides
477780-06-6D, AlexaFluor 633, conjugates with peptides
676540-33-3D, Eu-W 1284, conjugates with peptides
676540-54-8D, Eu-W 8184, conjugates with oligonucleotides
676540-55-9D, Eu-W 14014, conjugates with peptides
ROLE: ARG (Analytical reagent use); ANST (Analytical study);
USES (Uses)

(time-resolved fluorometric assays for **caspase**
-3, DNA helicase, and CD45 phosphatase employ Eu3+
chelates in conjunction with chromophore
quenchers)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD.

REFERENCE(S): (1) Beers, S; Bioorg Med Chem 1997, V5(12), P2201
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L25 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:892352 HCAPLUS

DOCUMENT NUMBER: 139:379989

ENTRY DATE: Entered STN: 14 Nov 2003

TITLE: Visualization and quantitation of cellular
cytotoxicity using cell-permeable **fluorogenic**
protease substrates and **caspase** activity

INVENTOR(S): indicator markers
 Packard, Beverly; Brown, Martin J.; Feinberg, Mark;
 Liu, Luzheng; Silvestri, Guido; Chahroudi, Ann;
 Komoriya, Akira
 PATENT ASSIGNEE(S): Oncolmmunin, Inc., USA
 SOURCE: U.S. Pat. Appl. Publ., 25 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: C12Q001-70
 SECONDARY: G01N033-53; G01N033-567; C12Q001-37
 US PATENT CLASSIF.: 435007200; 435023000; 435005000
 CLASSIFICATION: 15-1 (Immunochemistry)
 Section cross-reference(s): 9
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003211548	A1	20031113	US 2003-353791	20030128
PRIORITY APPLN. INFO.:			US 2002-353712P	P 20020129

ABSTRACT:

The disclosed invention provides a non-radioactive assay to monitor and quantify the target-cell killing activities mediated by cytotoxic T lymphocytes (CTLs), natural killer cells, and macrophages. This assay is predicated on the discovery that apoptosis pathway activation and, in particular, **caspase** activity, provides a measure of cytotoxic effector cell activity. In one embodiment, measurement of CTL-induced **caspase** activation in target cells is achieved via detection of the specific cleavage of **fluorogenic ***caspase***** substrates. This assay reliably detects antigen-specific CTL killing of target cells, and provides a more sensitive, more informative and safer alternative to the standard 51 Cr-release assay most often used to quantify CTL responses. The assay can be used to study CTL-mediated killing of primary host target cells of different cell lineages, and enables the study of antigen-specific cellular immune responses in real time at the single-cell level. As such, the assay can provide a valuable tool for studies of infectious disease pathogenesis and development of new vaccines and immunotherapies.

SUPPL. TERM: cell cytotoxicity **fluorogenic** protease substrate
caspase marker
 INDEX TERM: Proteins
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (GDP dissociation inhibitor, G4-GDI; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)
 INDEX TERM: Ribonucleoproteins
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (HnRNP-C1/2; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)
 INDEX TERM: Transcription factors
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (SREBP (sterol regulatory element-binding protein);

cellular cytotoxicity determination using cell-permeable
fluorogenic protease substrates and
caspase activity indicator markers)

INDEX TERM: Ribonucleoproteins
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (U1 snRNP (U1 snRNA-containing small nuclear ribonucleoprotein); cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Functional groups
 (aldehyde; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Infection
 (bacterial; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Labels
 (calorimetric; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Cytolysis
 (cell-mediated; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Cerebrospinal fluid
 Connective tissue
 Lymph
 (cell; cellular cytotoxicity determination using

cell-permeable
fluorogenic protease substrates and
caspase activity indicator markers)

INDEX TERM: Apoptosis
 Biomarkers (biological responses)
 Blood
 CD8-positive T cell
 Chromophores
Cyanine dyes
 Fibroblast
Fluorescent dyes
Fluorescent indicators
Fluorescent substances
 Immunization
 Immunotherapy
 Infection
 Lymphocytic choriomeningitis virus
 Macrophage
 Muscle
 Neoplasm
 Osteocyte
 Post-translational processing
 Transplant and Transplantation
 Vaccines
 (cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Actins
 Phycoerythrins

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: T cell (lymphocyte)
 (cytotoxic, MHC class I-restricted; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: T cell (lymphocyte)
 (cytotoxic, memory; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: T cell (lymphocyte)
 (cytotoxic; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Labels
 (enzymic; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Infection
 (exposure; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Cytometry
 (flow; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Labels
 (**fluorescent**; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Ligands
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (**fluorescent**; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Antibodies and Immunoglobulins
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (**fluorescently** labeled; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Indicators
 (**fluorogenic**; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Ligands
 ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
 (**fluorogenic**; cellular cytotoxicity determination using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Organelle

(granule; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Ketones, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(halo, ligands containing; cellular cytotoxicity
determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(huntingtin; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Functional groups
(hydrophobic; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Immunoassay
(immunofluorescence; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Animal cell
(inflammatory; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(lamins, nuclear; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Lymphocyte
(natural killer cell; cellular cytotoxicity determination
using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Nerve
(neuron; cellular cytotoxicity determination using
cell-permeable
fluorogenic protease substrates and
caspase activity indicator markers)

INDEX TERM: Labels
(radioactive; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Immunization
(vaccination; cellular cytotoxicity determination using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

INDEX TERM: Infection
(viral; cellular cytotoxicity determination using
cell-permeable
fluorogenic protease substrates and
caspase activity indicator markers)

INDEX TERM: 1239-45-8, Ethidium bromide 2321-07-5, **Fluorescein**
2768-89-0, **Rhodamine X** 7240-37-1,

7-Aminoactinomycin D 9001-92-7, Protease 9055-67-8, Poly
ADP ribose polymerase 13558-31-1, **Rhodamine** 110
20571-42-0, 7-**Diethylaminocoumarin** 25535-16-4,
Propidium iodide 70281-37-7, **Tetramethylrhodamine**
78990-62-2, Calpain 106178-18-1, Granzyme 122191-40-6,
Caspase 1 141436-78-4, Protein kinase C γ
169592-56-7, **Caspase** 3 179241-78-2,
Caspase 8 180189-96-2, **Caspase** 9
182372-14-1, **Caspase** 2 182372-15-2,
Caspase 6 186322-81-6, **Caspase**
189303-50-2, Cathepsin W 303752-61-6, DNA protein kinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)

(cellular cytotoxicity determination using cell-permeable
fluorogenic protease substrates and
caspase activity indicator markers)

INDEX TERM: 158475-79-7 160543-97-5 161928-86-5 202817-40-1
330153-12-3 330153-16-7 612835-70-8
612835-71-9 612835-72-0 612835-73-1 612835-74-2
612835-75-3 612835-76-4 612835-77-5 612835-78-6
612835-81-1

ROLE: PRP (Properties)

(unclaimed protein sequence; visualization and
quantitation of cellular cytotoxicity using
cell-permeable **fluorogenic** protease substrates
and **caspase** activity indicator markers)

L25 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:874871 HCAPLUS

DOCUMENT NUMBER: 139:360902

ENTRY DATE: Entered STN: 07 Nov 2003

TITLE: Homo-doubly **fluorophore**-labeled peptides for
the detection of enzyme activity in biological samples

INVENTOR(S): Packard, Beverly; Komoriya, Akira

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of Appl.
No. PCT/US00/24882.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN: C12Q001-68

SECONDARY: C12Q001-37; C07H021-04; C07K014-47; C12P021-02;
C12N005-06

US PATENT CLASSIF.: 435006000; 435023000; 435069100; 435320100; 435325000;
536023100; 530409000; 530410000; 530412000

CLASSIFICATION: 7-1 (Enzymes)

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003207264	A1	20031106	US 2000-747287	20001222
US 6037137	A	20000314	US 1997-802981	19970220
WO 2001018238	A1	20010315	WO 2000-US24882	20000911
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,			

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 WO 2002061038 A2 20020808 WO 2001-US49781 20011221
 WO 2002061038 C2 20021128
 WO 2002061038 A3 20030313
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 EP 1356084 A2 20031029 EP 2001-998079 20011221
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 PRIORITY APPLN. INFO.: US 1997-802981 A2 19970220
 US 1999-394019 A2 19990910
 WO 2000-US24882 A2 20000911
 US 2000-747287 A 20001222
 WO 2001-US49781 W 20011221

ABSTRACT:

The present invention provides for novel reagents whose **fluorescence** changes upon cleavage or a change in conformation of a backbone. The reagents comprise a backbone (e.g. nucleic acid, polypeptide, etc.) joining two **fluorophores** of the same species whereby the **fluorophores** form an H-dimer resulting in **quenching** of the **fluorescence** of the **fluorophores**. One such **fluorophore**-labeled peptide comprises DAIP(Nle)SIPKGY, where the **fluorophore** is linked to the N-terminus via the α -amino group of aspartic acid and to the ϵ -amino group of lysine by the displacement of a succinimidyl group linked to 6-**carboxytetramethylrhodamine** (6-TMR) or 5/6-carboxy-X-**rhodamine**. When the backbone is cleaved or changes conformation, the **fluorophores** are separated, no longer forming an H-type dimer, and are de-**quenched** thereby providing a detectable signal. The use of a single **fluorophore** rather than an "acceptor-donor" **fluorescence resonance** energy transfer system offers synthesis and performance advantages. An addnl. discovery of this invention is that attachment of a hydrophobic protecting group to a polypeptide enhances uptake of that polypeptide by a cell. A new class of profluorescent protease substrate was designed and synthesized with spectral properties that fit the exciton model.

SUPPL. TERM: **fluorophore** labeled peptide enzyme detection;
fluorescence quenching labeled peptide
 enzyme detection; proteinase detection **fluorescence**
quenching labeled peptide
 INDEX TERM: Antigens
 ROLE: ANT (Analyte); ANST (Analytical study)
 (detection of interaction with antibody; homo-doubly
fluorophore-labeled peptides for the detection of
 enzyme activity in biol. samples)
 INDEX TERM: Antibodies and Immunoglobulins
 ROLE: ANT (Analyte); ANST (Analytical study)
 (detection of interaction with antigen; homo-doubly
fluorophore-labeled peptides for the detection of

enzyme activity in biol. samples)
INDEX TERM: Agglutinins and Lectins
ROLE: ANT (Analyte); ANST (Analytical study)
(detection of interaction with carbohydrates; homo-doubly
fluorophore-labeled peptides for the detection of
enzyme activity in biol. samples)
INDEX TERM: Carbohydrates, analysis
ROLE: ANT (Analyte); ANST (Analytical study)
(detection of interaction with lectins; homo-doubly
fluorophore-labeled peptides for the detection of
enzyme activity in biol. samples)
INDEX TERM: Receptors
ROLE: ANT (Analyte); ANST (Analytical study)
(detection of interaction with ligand; homo-doubly
fluorophore-labeled peptides for the detection of
enzyme activity in biol. samples)
INDEX TERM: Nucleic acids
ROLE: ANT (Analyte); ANST (Analytical study)
(detection of interaction with nucleic acid-binding
proteins; homo-doubly **fluorophore**-labeled
peptides for the detection of enzyme activity in biol.
samples)
INDEX TERM: Ligands
ROLE: ANT (Analyte); ANST (Analytical study)
(detection of interaction with receptors; homo-doubly
fluorophore-labeled peptides for the detection of
enzyme activity in biol. samples)
INDEX TERM: Cytometry
(flow; homo-doubly **fluorophore**-labeled peptides
for the detection of enzyme activity in biol. samples)
INDEX TERM: Absorption spectroscopy
Animal tissue
Blood analysis
Confocal laser scanning microscopy
Cyanine dyes
Fluorescence microscopy
Fluorescence quenching
Fluorescent substances
Fluorometry
Lymph
Saliva
Urine analysis
Yeast
(homo-doubly **fluorophore**-labeled peptides for
the detection of enzyme activity in biol. samples)
INDEX TERM: Enzymes, analysis
ROLE: ANT (Analyte); ANST (Analytical study)
(homo-doubly **fluorophore**-labeled peptides for
the detection of enzyme activity in biol. samples)
INDEX TERM: Functional groups
(hydrophobic, cell permeation improvement with;
homo-doubly **fluorophore**-labeled peptides for
the detection of enzyme activity in biol. samples)
INDEX TERM: Animal cell
(insect; homo-doubly **fluorophore**-labeled
peptides for the detection of enzyme activity in biol.
samples)
INDEX TERM: Animal cell
(mammalian; homo-doubly **fluorophore**-labeled

peptides for the detection of enzyme activity in biol. samples)

INDEX TERM: Proteins
 ROLE: ANT (Analyte); ANST (Analytical study)
 (nucleic acid-binding, detection of interaction with nucleic acids; homo-doubly **fluorophore**-labeled peptides for the detection of enzyme activity in biol. samples)

INDEX TERM: 9004-06-2, Elastase 9026-81-7, Nuclease 169592-56-7, CPP32 protease
 ROLE: ANT (Analyte); ANST (Analytical study)
 (homo-doubly **fluorophore**-labeled peptides for the detection of enzyme activity in biol. samples)

INDEX TERM: 2321-07-5, **Fluorescein** 2768-89-0, **Rhodamine-X** 13558-31-1, **Rhodamine** 110 20571-42-0, 7-**Diethylaminocoumarin** 43070-85-5, **Hydroxycoumarin** 91809-67-5, 6-**Carboxytetramethylrhodamine** 203116-52-3
 212207-37-9 212207-40-4 212268-88-7 212268-91-2
 212268-95-6 212268-96-7 618892-30-1 618892-31-2
 618892-32-3 618892-33-4 618892-34-5 618892-35-6
 618892-36-7 618892-37-8 618892-38-9 618892-39-0
 618892-40-3 618892-41-4 618892-42-5 618892-43-6
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (homo-doubly **fluorophore**-labeled peptides for the detection of enzyme activity in biol. samples)

INDEX TERM: 119798-33-3 150234-52-9 150234-53-0 211872-23-0
 268202-35-3 288310-75-8 330153-28-1 330153-29-2
 330153-30-5 330153-31-6 330153-32-7 330153-34-9
 330153-37-2 330153-38-3 330153-39-4 **330153-40-7**
 330153-41-8 330153-42-9 330153-43-0 330153-44-1
 330153-45-2 330153-46-3 330153-47-4 330153-48-5
 330153-50-9 330153-51-0 330624-29-8 330624-30-1
 330624-31-2 330624-32-3 622400-72-0 622400-73-1
 622400-74-2 622400-75-3 622400-76-4 622400-77-5
 622400-78-6 622400-79-7 622400-80-0 622400-81-1
 622400-82-2 622400-83-3 622400-84-4 622400-85-5
 622400-86-6 622400-87-7 622400-88-8 622400-89-9
 622400-90-2 622400-91-3 622400-92-4 622400-93-5
 622400-94-6 622400-95-7 622400-96-8 622400-97-9
 622400-98-0 622400-99-1 622401-00-7 622401-01-8
 622401-02-9 622401-03-0 622401-04-1 622401-05-2
 622401-06-3 622401-07-4 622401-08-5 622401-09-6
 622401-10-9 622401-11-0 622401-12-1 622401-13-2
 622401-14-3 622401-15-4 622401-16-5 622401-17-6
 622401-18-7 622401-19-8 622401-20-1 622401-21-2
 622401-22-3 622401-23-4 622401-24-5 622401-25-6
 622401-26-7 622401-27-8 622401-28-9 622401-29-0
 ROLE: PRP (Properties)
 (unclaimed sequence; homo-doubly **fluorophore**-labeled peptides for the detection of enzyme activity in biol. samples)

L25 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 2003:818208 HCAPLUS
 DOCUMENT NUMBER: 139:322261
 ENTRY DATE: Entered STN: 17 Oct 2003
 TITLE: Visualization and quantitation of cellular

cytotoxicity using cell-permeable **fluorogenic**
protease substrates and **caspase** activity
indicator markers

INVENTOR(S): Packard, Beverly S.; Brown, Martin J.; Feinberg, Mark;
Liu, Luzheng; Silvestri, Guido; Chahroudi, Ann;
Komoriya, Akira
PATENT ASSIGNEE(S): Oncoimmunin, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A01N063-00
SECONDARY: A61K045-00; C12N005-00; C12Q001-02
CLASSIFICATION: 15-1 (Immunochemistry)
Section cross-reference(s): 9
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084333	A1	20031016	WO 2003-US2583	20030129
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-353112P P 20020129

ABSTRACT:

This invention provides a non-radioactive assay to monitor and quantify the target-cell killing activities mediated by cytotoxic T lymphocytes (CTLs). This assay is predicated on the discovery that apoptosis pathway activation and, in particular, **caspase** activity, provides a measure of cytotoxic effector cell activity. In one embodiment, measurement of CTL-induced *****caspase***** activation in target cells is achieved through detection of the specific cleavage of **fluorogenic caspase** substrates. This assay reliably detects antigen-specific CTL killing of target cells, and provides a more sensitive, more informative and safer alternative to the standard ⁵¹Cr-release assay most often used to quantify CTL responses. The assay can be used to study CTL-mediated killing of primary host target cells of different cell lineages, and enables the study of antigen-specific cellular immune responses in real time at the single-cell level. As such, the assay can provide a valuable tool for studies of infectious disease pathogenesis and development of new vaccines and immunotherapies.

SUPPL. TERM: immunocyte cytotoxicity **fluorogenic** substrate
protease **caspase**
INDEX TERM: Transcription factors
ROLE: ARG (Analytical reagent use); ANST (Analytical study);
USES (Uses)
(SREBP (steroid-responsive element-binding protein);
visualization and quantitation of cellular cytotoxicity
using **caspase** cleavage of)

INDEX TERM: Ribonucleoproteins
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (U1 snRNP (U1 snRNA-containing small nuclear ribonucleoprotein); visualization and quantitation of cellular cytotoxicity using **caspase** cleavage of)

INDEX TERM: Annexins
 ROLE: ARU (Analytical role, unclassified); ANST (Analytical study)
 (V, labeled; in visualization and quantitation of cellular cytotoxicity)

INDEX TERM: Animal cell
 Blood cell
 Bone
 Connective tissue
 Fibroblast
 Neoplasm
 (as target cell in visualization and quantitation of cellular cytotoxicity using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Chromophores
Fluorescent substances
 (**caspase** substrates-containing; in visualization and quantitation of cellular cytotoxicity)

INDEX TERM: T cell (lymphocyte)
 (cytotoxic, memory; visualization and quantitation of cellular cytotoxicity using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: T cell (lymphocyte)
 (cytotoxic; visualization and quantitation of cellular cytotoxicity using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Antigens
 ROLE: ANT (Analyte); BSU (Biological study, unclassified);
 ANST (Analytical study); BIOL (Biological study)
 (exoantigens; visualization and quantitation of cellular cytotoxicity using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers in target cells with expression of)

INDEX TERM: Muscle
 (fiber; as target cell in visualization and quantitation of cellular cytotoxicity using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Cytometry
 (flow; visualization and quantitation of cellular cytotoxicity using cell-permeable **fluorogenic** protease substrates and **caspase** activity indicator markers)

INDEX TERM: Ribonucleoproteins
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (hnRNP C (heterogeneous nuclear ribonucleoprotein C); visualization and quantitation of cellular cytotoxicity using **caspase** cleavage of)

INDEX TERM: Proteins
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (huntingtin; visualization and quantitation of cellular
 cytotoxicity using **caspase** cleavage of)

INDEX TERM: Formyl group
 (in visualization and quantitation of cellular
 cytotoxicity)

INDEX TERM: Proteins
 ROLE: ANT (Analyte); ANST (Analytical study)
 (lamins; visualization and quantitation of cellular
 cytotoxicity using **fluorophore**-labeled
 monoclonal antibodies to)

INDEX TERM: Antibodies and Immunoglobulins
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (monoclonal, labeled, with **fluorophores**; in
 visualization and quantitation of cellular cytotoxicity)

INDEX TERM: Lymphocyte
 (natural killer cell; visualization and quantitation of
 cellular cytotoxicity using cell-permeable
fluorogenic protease substrates and
caspase activity indicator markers)

INDEX TERM: Nerve
 (neuron; as target cell in visualization and
 quantitation of cellular cytotoxicity using
 cell-permeable **fluorogenic** protease substrates
 and **caspase** activity indicator markers)

INDEX TERM: **Cyanine** dyes
 (protease substrates-containing; in visualization and
 quantitation of cellular cytotoxicity)

INDEX TERM: Phycoerythrins
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (protease substrates-containing; in visualization and
 quantitation of cellular cytotoxicity)

INDEX TERM: Actins
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (visualization and quantitation of cellular cytotoxicity
 using **caspase** cleavage of)

INDEX TERM: Apoptosis
 Cytolysis
 Cytotoxicity
Fluorescence microscopy
 Human
 Macrophage
 (visualization and quantitation of cellular cytotoxicity
 using cell-permeable **fluorogenic** protease
 substrates and **caspase** activity indicator
 markers)

INDEX TERM: Transplant rejection
 (visualization and quantitation of cellular cytotoxicity
 using cell-permeable **fluorogenic** protease
 substrates and **caspase** activity indicator
 markers in relation to)

INDEX TERM: Vaccines
 (visualization and quantitation of cellular cytotoxicity
 using cell-permeable **fluorogenic** protease

substrates and **caspase** activity indicator
 markers in relation to screening for antigens for)

INDEX TERM: Animal virus
 Eubacteria
 Pathogen
 (visualization and quantitation of cellular cytotoxicity
 using cell-permeable **fluorogenic** protease
 substrates and **caspase** activity indicator
 markers in target cells infected with)

INDEX TERM: 186322-81-6, **Caspase**
 ROLE: BSU (Biological study, unclassified); BIOL (Biological
 study)
 (**fluorophore**-labeled inhibitors; in
 visualization and quantitation of cellular cytotoxicity)

INDEX TERM: 2321-07-5D, **Fluorescein**, protease
 substrates-containing 2768-89-0D, **Rhodamine-X**,
 protease substrates-containing 13558-31-1D, **Rhodamine**
 110, protease substrates-containing 20571-42-0D, 7-
Diethylaminocoumarin, protease substrates-containing
 70281-37-7D, **Tetramethylrhodamine**, protease
 substrates-containing
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (in visualization and quantitation of cellular
 cytotoxicity)

INDEX TERM: 1239-45-8, Ethidium bromide 7240-37-1, 7-Amino actinomycin
 D 25535-16-4, Propidium iodide
 ROLE: ARU (Analytical role, unclassified); ANST (Analytical
 study)
 (in visualization and quantitation of cellular
 cytotoxicity)

INDEX TERM: 158475-79-7 160543-97-5 161928-86-5 202817-40-1
 211918-90-0 220846-54-8 **330153-12-3**
 330153-16-7 612835-70-8 612835-71-9 612835-72-0
 612835-73-1 612835-74-2 612835-75-3 612835-76-4
 612835-77-5 612835-78-6 612835-79-7 612835-80-0
 612835-81-1
 ROLE: PRP (Properties)
 (unclaimed sequence; visualization and quantitation of
 cellular cytotoxicity using cell-permeable
fluorogenic protease substrates and
caspase activity indicator markers)

INDEX TERM: 141436-78-4, Protein kinase Cy 303752-61-6,
 DNA-dependent protein kinase
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (visualization and quantitation of cellular cytotoxicity
 using **caspase** cleavage of)

INDEX TERM: 78990-62-2, Calpain 106178-18-1, Granzyme 122191-40-6,
Caspase-1 169592-56-7, **Caspase-3**
 179241-78-2, **Caspase-8** 180189-96-2,
Caspase-9 182372-14-1, **Caspase-2**
 182372-15-2, **Caspase-6** 189303-50-2, Cathepsin W
 ROLE: ANT (Analyte); ANST (Analytical study)
 (visualization and quantitation of cellular cytotoxicity
 using cell-permeable **fluorogenic** protease
 substrates and **caspase** activity indicator
 markers)

INDEX TERM: 9055-67-8, Poly-ADP ribose polymerase

ROLE: ANT (Analyte); ANST (Analytical study)
(visualization and quantitation of cellular cytotoxicity
using **fluorophore**-labeled monoclonal antibodies
to)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD.

REFERENCE(S): (1) Bolton; US 20020058023 A1 2002
(2) Komoriya; US 6037137 A 2000 HCAPLUS
(3) Piwnica-Worms; US 6348185 B1 2002 HCAPLUS
(4) Robinson; US 6395889 B1 2002 HCAPLUS

L25 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:749309 HCAPLUS

DOCUMENT NUMBER: 140:213073

ENTRY DATE: Entered STN: 24 Sep 2003

TITLE: Ca²⁺-dependent and **caspase-3**-independent
apoptosis caused by damage in Golgi apparatus due to
2,4,5,7-**tetrabromorhodamine** 123
bromide-induced photodynamic effects

AUTHOR(S): Ogata, Maiko; Inanami, Osamu; Nakajima, Mihoko;
Nakajima, Takayuki; Hiraoka, Wakako; Kuwabara,
Mikiori

CORPORATE SOURCE: Laboratory of Radiation Biology, Department of
Environmental Veterinary Science, Graduate School of
Veterinary Medicine, Hokkaido University, Sapporo,
Japan

SOURCE: Photochemistry and Photobiology (2003), 78(3), 241-247
CODEN: PHCBAP; ISSN: 0031-8655

PUBLISHER: American Society for Photobiology

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 8-9 (Radiation Biochemistry)

ABSTRACT:

To clarify the role of the Golgi apparatus in photodynamic therapy-induced
apoptosis, its signaling pathway was studied after photodynamic treatment of
human cervix carcinoma cell line HeLa, in which a photosensitizer, 2,4,5,7-
tetrabromorhodamine 123 bromide (TBR), was incorporated into the Golgi
apparatus. Laser scanning microscopic anal. of TBR-loaded HeLa cells confirmed that
TBR was exclusively located in the Golgi apparatus. HeLa cells incubated with TBR
for 1 h were then exposed to visible light using an Xe lamp. Light of
wavelength below 670 nm was eliminated with a filter. Morphol. observation of
nuclei stained with Hoechst 33342 revealed that apoptosis of cells was induced
by exposure to light. ESR spectrometry showed that light-exposed TBR produced
both singlet oxygen (¹O₂) and superoxide anion (O₂⁻). Apoptosis induction by
TBR was inhibited by pyrrolidine dithiocarbamate, an O₂⁻ scavenger, but not by
NaN₃, a **quencher** of ¹O₂. Furthermore, TBR-induced apoptosis was
inhibited by aurintricarboxylic acid and ZnCl₂, which are known as inhibitors
of DNase (DNase) γ , and (acetoxymethyl)-1,2-bis(o-aminophenoxy)-ethane-
N,N,N',N'-tetraacetic acid, a chelator of Ca²⁺, but not by acetyl
Asp-Glu-Val-Asp-aldehyde, an inhibitor of **caspase-3**. These results
suggested that O₂⁻ was responsible for TBR-induced apoptosis, and
Ca²⁺-dependent and **caspase-3**-independent nuclease such as DNase
 γ played an important role in apoptotic signaling triggered by Golgi
dysfunction.

SUPPL. TERM: Golgi calcium **caspase** DNase PDT apoptosis
carcinoma

INDEX TERM: Antitumor agents
Apoptosis

Golgi apparatus
Human
Oxidative stress, biological
Photodynamic therapy
Photosensitizers (pharmaceutical)
(Golgi apparatus, calcium, **caspase**, and DNase role
in PDT-induced apoptosis in cervical carcinoma)

INDEX TERM: Uterus, neoplasm
(cervix, carcinoma; Golgi apparatus, calcium, **caspase**
, and DNase role in PDT-induced apoptosis in cervical
carcinoma)

INDEX TERM: 7440-70-2D, Calcium, ions, biological studies 9003-98-9,
DNase γ 169592-56-7, **Caspase 3**
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(Golgi apparatus, calcium, **caspase**, and DNase role
in PDT-induced apoptosis in cervical carcinoma)

INDEX TERM: 11062-77-4, Superoxide anion
ROLE: BSU (Biological study, unclassified); FMU (Formation,
unclassified); BIOL (Biological study); FORM (Formation,
nonpreparative)
(Golgi apparatus, calcium, **caspase**, and DNase role
in PDT-induced apoptosis in cervical carcinoma)

INDEX TERM: 7782-44-7, Oxygen, biological studies
ROLE: BSU (Biological study, unclassified); FMU (Formation,
unclassified); BIOL (Biological study); FORM (Formation,
nonpreparative)
(singlet; Golgi apparatus, calcium, **caspase**, and
DNase role in PDT-induced apoptosis in cervical
carcinoma)

INDEX TERM: 623903-26-4, **Tetrabromorhodamine 123**
ROLE: DMA (Drug mechanism of action); PAC (Pharmacological
activity); PKT (Pharmacokinetics); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(**tetrabromorhodamine 123**; Golgi apparatus, calcium,
caspase, and DNase role in PDT-induced apoptosis
in cervical carcinoma)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS
RECORD.

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L25 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:241895 HCAPLUS
 DOCUMENT NUMBER: 138:250716
 ENTRY DATE: Entered STN: 28 Mar 2003
 TITLE: Construction of combinatorial libraries of protease
 fluorogenic substrates and application to substrate
 profile determination
 INVENTOR(S): Backes, Bradley J.; Harris, Jennifer Leslie
 PATENT ASSIGNEE(S): IRM, LLC, Bermuda
 SOURCE: U.S. Pat. Appl. Publ., 26 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 INT. PATENT CLASSIF.:
 MAIN: G01N033-53
 SECONDARY: C12Q001-37; C07K007-06; C07K007-08
 US PATENT CLASSIF.: 435007100; 435023000; 530324000
 CLASSIFICATION: 7-3 (Enzymes)
 Section cross-reference(s): 34
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003059847	A1	20030327	US 2002-229950	20020827
WO 2003029823	A1	20030410	WO 2002-US27357	20020827

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
 RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-315116P P 20010827

ABSTRACT:

Non-peptide protease substrate libraries and high purity protease substrate libraries are constructed using fluorogenic compds. Preparation of the fluorogenic protease substrates is described. The libraries are useful in obtaining substrate profiles for a variety of proteases, such as methods for determining both prime and non-prime protease recognition sequences.

SUPPL. TERM: protease substrate combinatorial library fluorogenic compd
 INDEX TERM: Peptides, preparation
 ROLE: MSC (Miscellaneous); SPN (Synthetic preparation); PREP (Preparation)
 (Fmoc-based peptide synthesis; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Linking agents
 (ammonia-cleavable, in fluorogenic substrate synthesis; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Acids, reactions
 Bases, reactions
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (base-labile protecting group, in fluorogenic substrate synthesis; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Combinatorial library
 Enzyme kinetics
 (construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Proteins
 ROLE: MSC (Miscellaneous)
 (fluorogenic substrate containing; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Protective groups
 (in fluorogenic substrate synthesis; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Heterocyclic compounds
 ROLE: MSC (Miscellaneous)
 (moiety, protease substrate containing; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Fluorescence
 Fluorescence excitation
 Immobilization, molecular or cellular
 (of fluorogenic compound; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: Solid phase synthesis
 (of protease substrate; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

carbamoylmethylcoumarin 502632-11-3,
 7-Amino-3-carbomoylmethyl-4-methylcoumarin
 ROLE: ARG (Analytical reagent use); BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 (construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: 56-84-8, L-Aspartic acid, reactions
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (fluorogenic substrate coupling with; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: 100-51-6, Benzylalcohol, reactions 107-21-1, 1,2-Ethanediol, reactions
 ROLE: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
 (linker, in fluorogenic substrate synthesis; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: 9001-92-7, Protease
 ROLE: ANT (Analyte); BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
 (protease; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: 28920-43-6, Fmoc-Cl
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (protecting group; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: 12794-10-4, Benzodiazepine
 ROLE: RCT (Reactant); RACT (Reactant or reagent)
 (solid phase synthesis, fluorogenic substrate preparation; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

INDEX TERM: 9002-88-4, Polyethylene 9003-05-8, Polyacrylamide
 9003-53-6, Polystyrene 25322-68-3, PEG
 ROLE: NUU (Other use, unclassified); USES (Uses)
 (solid support, in fluorogenic substrate synthesis; construction of combinatorial libraries of protease fluorogenic substrates and application to substrate profile determination)

L25 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:230990 HCAPLUS

DOCUMENT NUMBER: 139:285536

ENTRY DATE: Entered STN: 25 Mar 2003

TITLE: Single-molecule detection technologies in miniaturized high-throughput screening: Fluorescence intensity distribution analysis

AUTHOR(S): Hapts, Ulrich; Rudiger, Martin; Ashman, Stephen; Turconi, Sandra; Bingham, Ryan; Wharton, Charlotte; Hutchinson, Jonathan; Carey, Charlotte; Moore, Keith J.; Pope, Andrew J.

CORPORATE SOURCE: GlaxoSmithKline, Harlow, UK
 SOURCE: Journal of Biomolecular Screening (2003), 8(1), 19-33
 CODEN: JBISF3; ISSN: 1087-0571
 PUBLISHER: Sage Publications
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 CLASSIFICATION: 1-1 (Pharmacology)

ABSTRACT:

Single-mol. detection technologies are becoming a powerful readout format to support ultra-high-throughput screening. These methods are based on the anal. of fluorescence intensity fluctuations detected from a small confocal volume element. The fluctuating signal contains information about the mass and brightness of the different species in a mixture. The authors demonstrate a number of applications of fluorescence intensity distribution anal. (FIDA), which discriminates mols. by their specific brightness. Examples for assays based on brightness changes induced by **quenching**/dequenching of fluorescence, fluorescence energy transfer, and multiple-binding stoichiometry are given for important drug targets such as kinases and proteases. FIDA also provides a powerful method to extract correct biol. data in the presence of compound fluorescence.

SUPPL. TERM: miniaturized high throughput screening fluorescence analysis
 single mol detection; fluorescence intensity distribution
 analysis miniaturized high throughput drug screening

INDEX TERM: Fluorometry
 (FIDA (fluorescence intensity distribution anal.);
 single-mol. detection technol. in miniaturized
 high-throughput screening using fluorescence intensity
 distribution anal. (FIDA))

INDEX TERM: RNA
 ROLE: ANT (Analyte); ANST (Analytical study)
 (binding; single-mol. detection technol. in miniaturized
 high-throughput screening using fluorescence intensity
 distribution anal. (FIDA))

INDEX TERM: High throughput screening
 (drug; single-mol. detection technol. in miniaturized
 high-throughput screening using fluorescence intensity
 distribution anal. (FIDA))

INDEX TERM: Drug screening
 (high throughput; single-mol. detection technol. in
 miniaturized high-throughput screening using fluorescence
 intensity distribution anal. (FIDA))

INDEX TERM: Ras proteins
 ROLE: ANT (Analyte); ANST (Analytical study)
 (p21ras; single-mol. detection technol. in miniaturized
 high-throughput screening using fluorescence intensity
 distribution anal. (FIDA))

INDEX TERM: **Fluorescence resonance** energy transfer
 (single-mol. detection technol. in miniaturized
 high-throughput screening using fluorescence intensity
 distribution anal. (FIDA))

INDEX TERM: 9001-84-7, Phospholipase A2 62996-74-1, Staurosporine
 ROLE: ANT (Analyte); ANST (Analytical study)
 (binding; single-mol. detection technol. in miniaturized
 high-throughput screening using fluorescence intensity
 distribution anal. (FIDA))

INDEX TERM: 9001-78-9, Alkaline phosphatase 9025-26-7, Cathepsin D
 9031-72-5, Alcohol dehydrogenase 67382-96-1,
 Melanin-concentrating hormone 141349-89-5, p60Src tyrosine

kinase 169592-56-7, **Caspase-3**

ROLE: ANT (Analyte); ANST (Analytical study)

(single-mol. detection technol. in miniaturized
high-throughput screening using fluorescence intensity
distribution anal. (FIDA))

INDEX TERM:

58-85-5, Biotin 60-23-1, Mercaptoethylamine 2321-07-5,
Fluorescein 9013-20-1, Streptavidin 70281-37-7,

Tetramethylrhodamine 146368-16-3 189200-71-3,

Rhodamine green

ROLE: ARG (Analytical reagent use); ANST (Analytical study);

USES (Uses)

(single-mol. detection technol. in miniaturized
high-throughput screening using fluorescence intensity
distribution anal. (FIDA))

REFERENCE COUNT:

40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS
RECORD.

REFERENCE(S):

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V1, P3 HCAPLUS
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L25 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:578878 HCAPLUS
 DOCUMENT NUMBER: 138:165551
 ENTRY DATE: Entered STN: 05 Aug 2002
 TITLE: A homogeneous **caspase-3** activity assay using
 HTRF technology
 AUTHOR(S): Preaudat, M.; Ouled-Diaf, J.; Alpha-Bazin, B.; Mathis,
 G.; Mitsugi, T.; Aono, Y.; Takahashi, K.; Takemoto, H.
 CORPORATE SOURCE: Research and New Technologies, CIS Biointernational,
 Bagnols-sur-Ceze, Fr.
 SOURCE: Journal of Biomolecular Screening (2002), 7(3),
 267-274
 CODEN: JBISF3; ISSN: 1087-0571
 PUBLISHER: Mary Ann Liebert, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 CLASSIFICATION: 7-1 (Enzymes)
 Section cross-reference(s): 1

ABSTRACT:

Caspases are cysteine proteases presenting a conserved active site that cleaves protein substrates at a highly specific position. They are involved in different aspects of the active cell death pathway. Most of them act through proteolytic degrdns. of cellular components. This paper describes the assay development, assay validation, and screening for inhibitors of this enzyme, which could be potential drug candidates. The assay uses homogeneous time-resolved fluorescence based on energy transfer from europium cryptate as donor to cross-linked **allophycocyanin** as acceptor (XL665). A double-tagged substrate, biotinyl-.vepsiln.-aminocaproyl-L-aspartyl-L-glutamyl-L-valyl-L-aspartyl-L-alanylL-propyl-N.vepsiln.-(2,4-dinitrophenyl)-L-lysine-amide (biotin-X-DEVDAPK(dnp)-NH₂), is conjugated with streptavidin cryptate and anti-dnp-XL665 monoclonal antibody. The close proximity between donor and acceptor induces a specific time-resolved fluorescence signal. In the presence of enzyme activity, the substrate cleavage induces an unlinking of the two fluorescent probes and, subsequently, the disappearance of the specific signal as a result of loss of proximity. Expts. to optimize the reagent concentration, incubation times, precision, reproducibility, and robustness are discussed in comparison with a fluorometric method.

SUPPL. TERM: **caspase 3** HTRF detn inhibitor screening
 INDEX TERM: **Allophycocyanins**
 ROLE: ARG (Analytical reagent use); ANST (Analytical study);
 USES (Uses)
 (cross-linked; homogeneous **caspase-3** activity
 assay using HTRF technol. and application to inhibitor
 screening)
 INDEX TERM: Solubility
 (effect of solubility of peptide substrate on HTRF assay
 precision; homogeneous **caspase-3** activity assay
 using HTRF technol. and application to inhibitor
 screening)
 INDEX TERM: Drug screening
Fluorescence resonance energy transfer
 Fluorescent indicators

INDEX TERM: (homogeneous **caspase-3** activity assay using
HTRF technol. and application to inhibitor screening)
Antibodies and Immunoglobulins
ROLE: ARG (Analytical reagent use); ANST (Analytical study);
USES (Uses)
(monoclonal, anti-dnp-XL665, conjugates with biotinylated
labeled peptide and streptavidin cryptate; homogeneous
caspase-3 activity assay using HTRF technol. and
application to inhibitor screening)

INDEX TERM: 26093-31-2, 7-Amino-4-methyl **coumarin**
ROLE: ARG (Analytical reagent use); ANST (Analytical study);
USES (Uses)
(HTRF assay comparison with; homogeneous **caspase**
-3 activity assay using HTRF technol. and application to
inhibitor screening)

INDEX TERM: 184179-08-6
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(**caspase-3** inhibitor; homogeneous
caspase-3 activity assay using HTRF technol. and
application to inhibitor screening)

INDEX TERM: 497178-91-3 497178-92-4 497178-93-5
ROLE: ARG (Analytical reagent use); ANST (Analytical study);
USES (Uses)
(effect of solubility of peptide substrate on HTRF assay
precision; homogeneous **caspase-3** activity assay
using HTRF technol. and application to inhibitor
screening)

INDEX TERM: 169592-56-7, **Caspase-3**
ROLE: ANT (Analyte); ANST (Analytical study)
(homogeneous **caspase-3** activity assay using
HTRF technol. and application to inhibitor screening)

INDEX TERM: 9013-20-1D, Streptavidin, cryptate derivative, conjugates with
biotinylated labeled peptide and anti-dnp-XL665 monoclonal
antibody 23978-55-4D, streptavidin derivative, conjugates with
biotinylated labeled peptide and anti-dnp-XL665 monoclonal
antibody 128703-72-0 497178-90-2D, conjugates with
streptavidin cryptate and anti-dnp-XL665 monoclonal antibody
ROLE: ARG (Analytical reagent use); ANST (Analytical study);
USES (Uses)
(homogeneous **caspase-3** activity assay using
HTRF technol. and application to inhibitor screening)

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD.

REFERENCE(S): (1) Alpha, B; Angew Chem 1987, V26, P266
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V57, P2197 MEDLINE
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Screening 1997
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P279 HCAPLUS

L25 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:438549 HCAPLUS
DOCUMENT NUMBER: 138:21605
ENTRY DATE: Entered STN: 11 Jun 2002
TITLE: Mitochondrial permeability transition can be directly
monitored in living neurons
AUTHOR(S): Gillesen, T.; Grasshoff, C.; Szinicz, L.
CORPORATE SOURCE: Max-Planck-Institut of Psychiatry, Munich, 80804,
Germany
SOURCE: Biomedicine & Pharmacotherapy (2002), 56(4), 186-193
CODEN: BIPHEX; ISSN: 0753-3322
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 9-5 (Biochemical Methods)
Section cross-reference(s): 13

ABSTRACT:

Mitochondria have been suggested as key players in apoptotic cell death of neurons and many other tissues because the release of proapoptotic mols. from mitochondria is implicated in **caspase** activation. As a potential release mechanism, the occurrence of a large pore opening in the inner membrane (mitochondrial permeability transition pore, PTP) has been proposed, but has not yet been observed directly in neurons. We investigated whether the calcein/Co2+-**quenching** technique introduced by Petronilli et al. [Biofactors 8 (1998) 263], which allows direct observation of PTP opening, can be applied to neurons. Exposure of calcein-loaded neurons to Co2+ ions resulted in the fading of diffuse cytoplasmic calcein fluorescence, with organelle-restricted fluorescent spots remaining. These spots were colocalized with mitochondrially-entrapped **tetramethylrhodamineethylester** (TMRE) fluorescence and corresponded to colocalization of calcein and TMRE fluorescence in digitonin-permeabilized neurons. Importantly, extensive neuronal calcium loading, which is assumed to induce PTP opening, resulted in significant fading of mitochondrial fluorescence, suggesting the occurrence of a permeability transition. This fluorescence decrease could be completely prevented by the PTP blocker cyclosporin A.

SUPPL. TERM: mitochondria permeability transition pore opening neuron
calcein cobalt assay; PTP transport neuron calcein cobalt
tetramethylrhodamineethylester method
INDEX TERM: Pore
(PTP (permeability transition pore); mitochondrial
permeability transition pore (PTP) opening can be
directly monitored in living rat neurons using
calcein/Co2+-**quenching** technique)
INDEX TERM: Mitochondria
(mitochondrial permeability transition pore (PTP) opening

can be directly monitored in living rat neurons using calcein/Co2+-**quenching** technique)

INDEX TERM: Nerve
(neuron; mitochondrial permeability transition pore (PTP) opening can be directly monitored in living rat neurons using calcein/Co2+-**quenching** technique)

INDEX TERM: Biological transport
(permeation, via PTP; mitochondrial permeability transition pore (PTP) opening can be directly monitored in living rat neurons using calcein/Co2+-**quenching** technique)

INDEX TERM: 1461-15-0, Calcein 7440-48-4, Cobalt, biological studies
ROLE: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(mitochondrial permeability transition pore (PTP) opening can be directly monitored in living rat neurons using calcein/Co2+-**quenching** technique)

INDEX TERM: 139626-15-6, **Tetramethylrhodamineethyl ester**
ROLE: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(use in PTP opening assay; mitochondrial permeability transition pore (PTP) opening can be directly monitored in living rat neurons using calcein/Co2+-**quenching** technique)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Altschuld, R; Am J Physiol 1992, V262, PH1699 HCAPLUS
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L25 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:251430 HCAPLUS

DOCUMENT NUMBER: 135:32068

ENTRY DATE: Entered STN: 10 Apr 2001

TITLE: Febrile and acute hyperthermia enhance TNF-induced necrosis of murine L929 fibrosarcoma cells via **caspase**-regulated production of reactive

oxygen intermediates
 AUTHOR(S): Leroux, E.; Auzenne, E.; Weidner, D.; Wu, Z. Y.;
 Donato, N. J.; Klostergaard, J.
 CORPORATE SOURCE: Department of Molecular & Cellular Oncology, MD
 Anderson Cancer Center, The University of Texas,
 Houston, TX, 77030, USA
 SOURCE: Journal of Cellular Physiology (2001), 187(2), 256
 CODEN: JCLLAX; ISSN: 0021-9541
 PUBLISHER: Wiley-Liss, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 CLASSIFICATION: 14-1 (Mammalian Pathological Biochemistry)
 Section cross-reference(s): 15

ABSTRACT:

Previous studies have demonstrated the essential role of TNF-induced reactive oxygen intermediates (ROI) in the necrosis of L929 cells. The authors investigated the mol. basis for the interaction of hyperthermia and TNF in these cells. Hyperthermia, both febrile (40.0-40.5°) and acute (41.5-41.8°), strongly potentiated TNF killing, and sensitization was significantly **quenched** by the antioxidant, BHA. The broad-spectrum ***caspase*** inhibitor, Z-VAD, has been shown to markedly increase the TNF sensitivity of L929 cells at 37°; the authors observed that hyperthermia would also enhance the sensitivity of L929 cells to TNF + Z-VAD and that BHA could significantly **quench** the response, as well. The basis for hyperthermic potentiation was unlikely thermally-increased sensitivity to ROI, as treatment with hydrogen peroxide for 24 h killed L929 cells essentially equivalently, whether incubated continuously at 37° or at 40.0-40.5°, or for 2 h at 41.5-41.8°. However, febrile and acute hyperthermia markedly increased TNF-induced production of ROI, with or without Z-VAD. Hyperthermia dramatically accelerated the onset of this production, as well as the onset of necrotic death, as determined by oxidation of dihydro-rhodamine and propidium iodide staining, resp., both of which were significantly ***quenchable*** with BHA. The authors conclude that hyperthermia potentiates TNF-mediated killing in this cell model primarily by increasing the afferent, and not the efferent, phase of TNF-induced necrosis.

SUPPL. TERM: fever tumor necrosis factor fibrosarcoma **caspase**
 reactive oxygen; hyperthermia TNF fibrosarcoma necrosis
caspase reactive oxygen
 INDEX TERM: Sarcoma
 (fibrosarcoma; hyperthermia enhances TNF-induced necrosis
 fibrosarcoma cells via **caspase**-regulated production
 of reactive oxygen intermediates)
 INDEX TERM: Fever and Hyperthermia
 Hyperthermia (therapeutic)
 (hyperthermia enhances TNF-induced necrosis fibrosarcoma
 cells via **caspase**-regulated production of reactive
 oxygen intermediates)
 INDEX TERM: Reactive oxygen species
 Tumor necrosis factors
 ROLE: BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); BIOL (Biological
 study)
 (hyperthermia enhances TNF-induced necrosis fibrosarcoma
 cells via **caspase**-regulated production of reactive
 oxygen intermediates)
 INDEX TERM: 186322-81-6, **Caspase**
 ROLE: BPR (Biological process); BSU (Biological study,
 unclassified); BIOL (Biological study); PROC (Process)

(hyperthermia enhances TNF-induced necrosis fibrosarcoma cells via **caspase**-regulated production of reactive oxygen intermediates)

INDEX TERM: 7782-44-7, Oxygen, biological studies

ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(reactive; hyperthermia enhances TNF-induced necrosis fibrosarcoma cells via **caspase**-regulated production of reactive oxygen intermediates)

L25 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:185948 HCAPLUS

DOCUMENT NUMBER: 134:248826

ENTRY DATE: Entered STN: 16 Mar 2001

TITLE: **Fluorogenic** peptides for the detection of protease activity in biological samples and methods of their use

INVENTOR(S): Komoriya, Akira; Packard, Beverly S.

PATENT ASSIGNEE(S): Oncoimmunin, Inc., USA

SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:
MAIN: C12Q001-37
SECONDARY: G01N021-00; G01N021-76; A61K038-00

CLASSIFICATION: 7-1 (Enzymes)

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018238	A1	20010315	WO 2000-US24882	20000911
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1214445	A1	20020619	EP 2000-961782	20000911
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
JP 2003508080	T2	20030304	JP 2001-521773	20000911
US 2003207264	A1	20031106	US 2000-747287	20001222
US 2004096926	A1	20040520	US 2001-874350	20010604
PRIORITY APPLN. INFO.:			US 1999-394019	A 19990910
			US 1997-802981	A2 19970220
			WO 1998-US3000	A2 19980220
			WO 2000-US24882	W 20000911

OTHER SOURCE(S): MARPAT 134:248826

ABSTRACT:

The present invention provides for novel reagents whose **fluorescence** increases in the presence of particular proteases. The reagents comprise a characteristically folded peptide backbone conjugated to two **fluorophores** such that the **fluorophores** are located opposite

sides of a cleavage site. When the folded peptide is cleaved, as by digestion with a protease, the **fluorophores** provide a high intensity ***fluorescent*** signal at a visible wavelength. Because of their high ***fluorescence*** signal in the visible wavelengths, these protease indicators are particularly well suited for detection of protease activity in biol. samples, in particular in frozen tissue sections. Thus, this invention also provides for methods of detecting protease activity in situ in frozen sections.

SUPPL. TERM: **fluorogenic** peptide protease detn biol sample; in situ protease detn **fluorogenic** peptide; frozen tissue protease detn **fluorogenic** peptide

INDEX TERM: Cytometry
(flow; **fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

INDEX TERM: Absorption spectroscopy
Animal tissue
Blood analysis
Drug delivery systems
Fluorometry
Lymph
Saliva
Urine analysis
(**fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

INDEX TERM: Enzymes, analysis
ROLE: ANT (Analyte); ANST (Analytical study)
(**fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

INDEX TERM: Peptides, uses
ROLE: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

INDEX TERM: Animal cell
(mammalian, delivery of mols. to; **fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

INDEX TERM: Biological transport
(uptake; **fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

INDEX TERM: 9001-92-7, Protease 9004-06-2, Elastase 169592-56-7, CPP32 protease
ROLE: ANT (Analyte); ANST (Analytical study)
(**fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

INDEX TERM: 596-24-7D, 9-(2-Carboxyphenyl)-**xanthylum**, peptides containing 2768-89-0D, **Rhodamine X**, peptides containing 20571-42-0D, 7-**Diethylaminocoumarin**, peptides containing 25152-49-2D, 9-(2-Carboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino) **xanthylum**, peptides containing 25794-80-3D, 9-(2-Carboxyphenyl)-3,6-bis(ethylamino) **xanthylum**,

peptides containing 98181-63-6D, peptides containing
 119798-33-3D, **fluorogenic** peptides containing
 125481-77-8D, 9-(2,5-Dicarboxyphenyl)-3,6-bis-
 (dimethylamino)**xanthylum** chloride (5-TMR),
 peptides containing 135926-08-8D, 9-(2,6-Dicarboxyphenyl)-3,6-
 bis-(dimethylamino)**xanthylum** chloride (6-TMR),
 peptides containing 150234-52-9D, **fluorogenic**
 peptides containing 198978-94-8D, peptides containing
 203116-52-3 211872-23-0D, **fluorogenic** peptides
 containing 212207-37-9, 6-TMR-NorFes-6-TMR 212268-88-7
 212268-91-2 212268-95-6 212268-97-8 212268-98-9
 212268-99-0 212269-00-6 212269-01-7 212269-02-8
 212269-03-9 212269-04-0 212269-05-1 212269-06-2
 212269-07-3 212269-08-4 212269-09-5 212269-10-8
 288310-75-8D, **fluorogenic** peptides containing
 330152-87-9, 6-TMR-K-NorFes-6-TMR 330152-88-0D, peptides
 containing 330152-89-1D, peptides containing 330152-90-4D,
 peptides containing 330152-91-5D, peptides containing
 330152-92-6D, peptides containing 330152-93-7D, peptides
 containing 330152-94-8D, peptides containing 330152-95-9D,
 peptides containing 330152-96-0D, peptides containing
 330152-97-1D, peptides containing 330152-98-2D, peptides
 containing 330152-99-3D, peptides containing 330153-00-9D,
 peptides containing 330153-01-0D, peptides containing
 330153-02-1D, peptides containing 330153-03-2D, peptides
 containing 330153-04-3D, peptides containing 330153-05-4D,
 peptides containing 330153-06-5D, peptides containing
 330153-07-6D, peptides containing 330153-08-7D, peptides
 containing 330153-09-8D, peptides containing 330153-10-1D,
 peptides containing 330153-11-2D, peptides containing
330153-12-3D, peptides containing 330153-13-4D,
 peptides containing 330153-14-5D, peptides containing
 330153-15-6D, peptides containing 330153-16-7D, peptides
 containing 330153-17-8D, peptides containing 330153-18-9D,
 peptides containing 330153-19-0D, peptides containing
 330153-20-3D, peptides containing 330153-21-4D, peptides
 containing 330153-22-5D, peptides containing 330153-23-6D,
 peptides containing 330153-24-7D, peptides containing
 330153-25-8D, peptides containing 330153-26-9D,
 9-(2,6-Dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)
xanthylum, halides, peptides containing 330153-27-0D,
fluorogenic peptides containing 330153-28-1D,
fluorogenic peptides containing 330153-29-2D,
fluorogenic peptides containing 330153-30-5D,
fluorogenic peptides containing 330153-31-6D,
fluorogenic peptides containing 330153-32-7D,
fluorogenic peptides containing 330153-33-8D,
fluorogenic peptides containing 330153-34-9D,
fluorogenic peptides containing 330153-35-0D,
fluorogenic peptides containing 330153-36-1D,
fluorogenic peptides containing 330153-37-2D,
fluorogenic peptides containing 330153-38-3D,
fluorogenic peptides containing 330153-39-4D,
fluorogenic peptides containing **330153-40-7D**,
fluorogenic peptides containing 330153-41-8D,
fluorogenic peptides containing 330153-42-9D,
fluorogenic peptides containing 330153-43-0D,
fluorogenic peptides containing 330153-44-1D,
fluorogenic peptides containing 330153-45-2D,

fluorogenic peptides containing 330153-46-3D,
fluorogenic peptides containing 330153-47-4D,
fluorogenic peptides containing 330153-48-5D,
fluorogenic peptides containing 330153-49-6D,
fluorogenic peptides containing 330153-50-9D,
fluorogenic peptides containing 330153-51-0D,
fluorogenic peptides containing 330443-38-4,
 6-TMR-K-NorFes-DER 330443-39-5D, 9-(2,5 Or
 2,6-Dicarboxyphenyl)-2,7-dimethyl-3,6-bisamino
xanthylum (Rh110), peptides containing 330443-40-8D,
 9-(2,5 Or 2,6-Dicarboxyphenyl)-2,7-dimethyl-3-amino-6-hydroxy-
xanthylum (Blue Rh), peptides containing
 ROLE: ARG (Analytical reagent use); BPR (Biological
 process); BSU (Biological study, unclassified); ANST
 (Analytical study); BIOL (Biological study); PROC (Process);
 USES (Uses)
 (fluorogenic peptides for the detection of
 protease activity in biol. samples and methods of their
 use)

INDEX TERM:

330574-44-2	330574-45-3	330624-26-5	330624-27-6
330624-28-7	330624-29-8	330624-30-1	330624-31-2
330624-32-3	330658-97-4	330659-14-8	330659-15-9
330659-16-0	330659-17-1	330659-18-2	330659-19-3
330659-20-6	330659-21-7	330659-22-8	330659-23-9
330659-24-0	330659-25-1	330659-26-2	330659-27-3
330659-28-4	330659-29-5	330659-30-8	330659-31-9
330659-32-0	330659-33-1	330659-35-3	330659-36-4
330659-38-6	330659-39-7	330659-40-0	330659-41-1
330659-42-2	330659-44-4	330659-45-5	330659-46-6
330659-47-7	330659-48-8	330659-49-9	330659-50-2
330659-52-4	330659-53-5	330659-58-0	330659-59-1
330812-07-2	330812-08-3	330812-09-4	330812-10-7
330812-11-8	330812-12-9	330812-24-3	330812-25-4
330812-26-5	330812-27-6	330812-28-7	330812-29-8
330812-30-1	330812-31-2	330812-32-3	330812-33-4
330812-34-5	330812-35-6	330812-36-7	330812-37-8
330812-47-0	330812-48-1	330812-49-2	330812-50-5
330812-51-6	330812-56-1	330812-57-2	330812-58-3
330812-59-4	330812-63-0	330812-64-1	330812-65-2
330812-67-4	330812-76-5	330812-82-3	330812-83-4
330812-84-5	330812-85-6	330812-86-7	330812-87-8
330812-88-9	330813-01-9	330813-02-0	330813-03-1
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330813-21-3	330813-23-5	330813-32-6	330813-39-3
330813-40-6	330813-41-7	330813-42-8	330813-43-9
330813-44-0	330813-45-1	330813-46-2	330813-48-4
330813-49-5	330813-51-9	330813-52-0	330813-53-1
330813-57-5	330813-58-6	330813-59-7	330813-60-0
330813-61-1	330813-62-2	330813-63-3	330813-64-4
330813-68-8	330813-69-9	330813-74-6	330813-75-7
330813-84-8	330813-88-2	330813-89-3	330813-90-6
330813-91-7	330813-94-0	330813-95-1	330813-96-2
330813-97-3	330813-98-4	330813-99-5	330814-00-1
330814-01-2	330814-02-3	330814-03-4	330814-04-5
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330814-09-0	330814-10-3	330814-12-5	330814-13-6

330970-84-8 330970-95-1 330974-77-1 330974-80-6
 330974-94-2 330975-04-7 330975-05-8 330975-14-9
 330975-19-4 330975-20-7 330975-21-8 330975-23-0
 330975-24-1 330975-25-2 330975-26-3 330975-27-4
 330975-28-5 330975-30-9

ROLE: PRP (Properties)

(unclaimed sequence; **fluorogenic** peptides for the detection of protease activity in biol. samples and methods of their use)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Dykstra; US 5723288 A 1998 HCAPLUS
 (2) Komoriya; US 6037137 A 2000 HCAPLUS
 (3) Schade; US 5804395 A 1998 HCAPLUS

L25 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:815094 HCAPLUS

DOCUMENT NUMBER: 133:360594

ENTRY DATE: Entered STN: 21 Nov 2000

TITLE: New fluorescent probe possessing fluorescent substances on both ends of peptide substrate for detecting **caspase** activity through **fluorescence resonance** energy transfer

INVENTOR(S): Nagano, Tetsuo; Kikuchi, Kazuya; Minakami, Susumu

PATENT ASSIGNEE(S): Foundation for Scientific Technology Promotion, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

INT. PATENT CLASSIF.:

MAIN: C12Q001-37

SECONDARY: C07K001-13; C07K007-06; G01N021-78

CLASSIFICATION: 9-5 (Biochemical Methods)

Section cross-reference(s): 7

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000316598	A2	20001121	JP 1999-134476	19990514
PRIORITY APPLN. INFO.:			JP 1999-134476	19990514

ABSTRACT:

A new fluorescent probe is provided so that the **caspase** activity is detected by observing the time course of the ratio of the relative fluorescence intensity between two fluorescent groups (D and A) bound to the both ends of the peptide substrate possessing the amino acid sequence (e.g., -GDEVDGVK-, -AYVHDAPVK-) to be specifically cleaved by **caspase**. The combination of the two fluorescent groups is chosen so that the fluorescence spectrum of the fluorescent group D (e.g., lucifer yellow, 6-carboxydichlorofluorescein) excited with visible light overlaps the excitation spectrum of the fluorescent group A (e.g., 5-carboxytetramethylrhodamine, 5-carboxy-X-***rhodamine***), and therefore, the **fluorescence resonance** energy transfer takes place between the two fluorescent groups separated with the amino acid sequence less than 100Å long.

SUPPL. TERM: fluorescent probe **caspase** peptide substrate sequence; **fluorescence resonance** energy transfer imaging **caspase**

INDEX TERM: . **Resonant** energy transfer
 (fluorescence; new fluorescent probe possessing
 fluorescent substances on both ends of peptide substrate
 for detecting **caspase** activity through
fluorescence resonance energy transfer)

INDEX TERM: Imaging
 (fluorescent; new fluorescent probe possessing
 fluorescent substances on both ends of peptide substrate
 for detecting **caspase** activity through
fluorescence resonance energy transfer)

INDEX TERM: Apoptosis
 Fluorescence excitation
 Fluorescent probes
 Fluorescent substances
 Protein sequences
 (new fluorescent probe possessing fluorescent substances
 on both ends of peptide substrate for detecting
caspase activity through **fluorescence**
resonance energy transfer)

INDEX TERM: Peptides, reactions
 ROLE: PEP (Physical, engineering or chemical process); RCT
 (Reactant); PROC (Process); RACT (Reactant or reagent)
 (new fluorescent probe possessing fluorescent substances
 on both ends of peptide substrate for detecting
caspase activity through **fluorescence**
resonance energy transfer)

INDEX TERM: 169592-56-7, **Caspase-3** 186322-81-6,
Caspase
 ROLE: BAC (Biological activity or effector, except adverse);
 BSU (Biological study, unclassified); BIOL (Biological
 study)
 (new fluorescent probe possessing fluorescent substances
 on both ends of peptide substrate for detecting
caspase activity through **fluorescence**
resonance energy transfer)

INDEX TERM: 82446-52-4, Lucifer yellow 91809-66-4 216699-35-3
 307926-47-2 307926-48-3 307926-49-4
 ROLE: PEP (Physical, engineering or chemical process); RCT
 (Reactant); PROC (Process); RACT (Reactant or reagent)
 (new fluorescent probe possessing fluorescent substances
 on both ends of peptide substrate for detecting
caspase activity through **fluorescence**
resonance energy transfer)



Creation date: 06-28-2004
Indexing Officer: NGOLSON - NA-WAL GOLSON
Team: OIPEScanning
Dossier: 09394019

Legal Date: 06-23-2004

No.	Doccode	Number of pages
1	SRNT	4

Total number of pages: 4

Remarks:

Order of re-scan issued on